## REMARKS

Claims 1-6, 8-14, 17-19, 48, 50, 58 and 59 are pending in the instant application. Applicants have amended claim 1 to further clarify the claim. Claim 1 was amended to indicate that the cells of the immune system encounter the antigen within the device of the current invention. This amendment is supported by the specification at page 14, lines 2-5, and therefore, no new matter has been added by this amendment which is fully supported by the specification and claims as originally filed. Entry of the amendment and the remarks made herein into the record for the above-identified application is respectfully requested.

## 1. THE REJECTION FOR NONSTATUTORY OBVIOUSNESS-TYPE DOUBLE PATENTING SHOULD BE WITHDRAWN

Claims 1-6, 8-14, 17-19, 48, 50, and 58-59 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 57-76 of copending Application No. 10/783,052. The Examiner contends that although the claims of the two applications are not identical, the current claims would have been obvious to one skilled in the art in light of the '052 application.

In response, and without agreeing with the double patenting rejection, Applicants intend to submit an appropriate Terminal Disclaimer once the claims are indicated to be allowable in the present application but for a Terminal Disclaimer. In the meanwhile, Applicants request that the double patenting rejection be held in abeyance.

## 2. THE REJECTION FOR OBVIOUSNESS UNDER 35 U.S.C. § 103(a) SHOULD BE WITHDRAWN

Claims 1-6, 8-14, 17-19, 48, 50, and 58-59 are rejected under 35 USC § 103(a) as being obvious in light of Barr et al. ("Barr"), U.S. Patent No. 5,593,697, in view of Andrianov et al. ("Andrianov"), U.S. Patent No. 5,529,777. Specifically, the Examiner alleges that Barr teaches a pharmaceutical implant comprising a water insoluble material containing an antigen within a polymer coat. Further, the Examiner addresses the Applicants' previous assertion that Barr fails to

render the present invention obvious because it did not contain a diffusion barrier by asserting that "one is actually present in the device." And further asserting that the rupture of the device is "irrelevant" considering that it occurs well after 10 days and the current application discloses that the device is biodegradable. Lastly, the Examiner relies upon *In re Spada*, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990) for the principle that products of identical chemical compositions can not have mutually exclusive properties in support of the assertion that Barr renders the current invention obvious given the suggestion that similar polymers may be used within the inventions. The Applicants respectfully disagree with the Examiner.

As Applicants have noted previously, the present invention relates to an implantable device that mimics the activity of a lymph node in order to modulate the immune response in a mammal to an antigen. (Page 13, Lines 17-18). The efficacy of this organ in the body's immune system is in part due to the high concentration of agents that accumulate within the lymph node and of lymphocytes and macrophages present within the lymph node.

The present invention replicates this environment within a novel implant made of a porous matrix impregnated or injected with the antigen contained within a perforated but otherwise impermeable container. (Page 4, Lines 12-15). The container acts as a diffusion barrier: maintaining within the device the antigen and high levels of cytokines and other co-stimulatory factors produced by immune cells that enter the device which in turn enhance the response of subsequent immune cells that enter the device. (Page 4, Line 21 to Page 5, Line 1). This interaction of the antigen present in the device and the immune cells and co-stimulatory molecules within the device provides an enhanced immune response to the antigen, as well as imparts long term immunity by producing a population of memory cells. (Page 14, line 9-11). Thus, the diffusion barrier generated by the perforated but otherwise impermeable container permits the device to produce an immune response to the antigen similar to that generated by the lymph nodes within the body. (Page 12, Lines 3-6). Also the specification notes that the device of the current invention may be made of biodegradable material so that the container and matrix begin to significantly biodegrade after the useful life of the device, about 10 days after implantation when the immune cell population has egressed from the device and it is no longer functional. (Page 22, lines 13-16 and Page 24, lines 2-5).

The Barr device is concerned with a biocompatible or biodegradable implant for the

administration of antigens in a pulse released fashion, in which the antigen contacts tissue in the host animal, at a period of time after implantation. (Col. 1, lines 7-11). The Barr device is comprised of (a) a biologically active material, (b) an excipient comprising at least one water soluble material and at least one water insoluble material, and (c) a polymer film coating adapted to rupture at a predetermined time after implantation. (Col. 3, lines 30-42). According to Barr, the polymer film is a biocompatible bilayer film capable of forming an impermeable barrier to the antigen (isolating the antigen from physiological fluid) until the inner layer of the film fails. (Col. 5, lines 2-5). Specifically, the polymer film consists of an insoluble outer layer, whose thickness controls the timing and degree of access of physiological fluid to the inner layer, and an inner layer, which is soluble at physiological pH. (Col. 5, lines 5-11). The failure of the inner layer of the film permits the physiological fluid to access the excipient, which according to Barr consists of water soluble and insoluble excipients. The water insoluble excipient acts as a swellable excipient which exerts pressure sufficient enough to rupture the impermeable outer film. (Col. 5, lines 11-14.)

Several distinctions between the Barr device and the current invention are apparent from the above disclosures: (1) the method of inducing an immune response; (2) the existence of a diffusion barrier; and (3) the reason for incorporating biocompatible or biodegradable polymers into the structure of the devices.

First, the means for inducing an immune response differs between Barr and the current invention. As is explicitly disclosed within Barr, the antigen is released from the device where it is placed in contact with the tissues of the recipient of the implant. In contrast, the central purpose of the current invention is to emulate a lymph node by bringing immune cells into contact with the antigen within the device so as to enhance the immune response. The Examiner argues that it is intuitive that the Barr device would attract immune cells; however, there is no teaching within Barr that the immune cells would enter the Barr device. Moreover, Barr teaches the release of antigen from the Barr device so that the antigens come into contact with the recipient's tissues: splitting (Col. 5, line 32) or rupture (Col. 8, line 31) of the polymer film causes release of the payload antigen (Col. 6, lines 20-21), and therefore it would not be obvious to one of skill in the art to have the immune response to the antigen occur within the device as is taught by the current invention. Barr notes that formation of holes in the film (as a result of certain copolymers) during preparation is undesirable and favors a partially erodable film (Col. 6, lines 26-33). The films are impermeable to water soluble compounds with a molecular weight > 1000 Daltons until the polymer partially

hydrolyzes, forming pores that permits release of the antigen (Col. 6, lines 38-43). In contrast, the current invention comprises holes and is otherwise impermeable to water soluble compounds as well as water. Applicants have amended claim 1 to clarify that the antigen comes into contact with the immune cells within the device as opposed to outside of the device as is taught by Barr.

Next, and related to the first point, Barr does not contain a diffusion barrier as taught by the current invention. As noted in the specification of the above-noted application, the perforated container maintains the diffusion barrier, *i.e.* the perforations in the container restrict the diffusion of antigens from the device but permit the free ingress and egress of immune and other cells out of the device. (pg. 14, lines 2-7). Whereas the outer film in the Barr device forms an impermeable barrier to the antigen until such time as the inner, pH sensitive film fails due to ingress of physiological fluid (i.e., molecular weight below 1000 Daltons; Col. 6, lines 39-40). According to Barr, the thickness of this outer barrier may be varied to adjust the time to failure of the inner film. Thus, the bilayer film in the Barr device does not operate to the same effect as the perforated container in the current device. The bilayer film in the Barr device acts as a timing device by permitting the release of antigen at a point in the future when the film fails, whereas the perforated container in the current invention acts as a selective barrier permitting during its operation the ingress and egress of immune cells within the device while restricting the release of antigen from the device during the useful life of the device. Furthermore, one of ordinary skill in the art would not think to replace the bilayer film of the Barr device with the "diffusion barrier" of the current invention given that there is no teaching in Barr of an immune response occurring with in the device since Barr teaches the release of the antigen from the device.

Lastly, the Examiner bases the current rejection to a large extent on the fact that Barr and the current invention teach that similar biocompatible and biodegradable polymers may be used within the devices. The Examiner concludes that since the polymers will have the same attributes the devices themselves will function in the same manner. Such a conclusion is false. Although the polymers will have the same attributes, the Barr device and current device have been designed to achieve different ends: the timed release of antigen in Barr and the creation of a controlled environment to enhance the immune response similar to a lymph node in the current invention. The Barr device relies upon the biodegradable polymers to provide for the controlled failure (rupture) of the outer film so that the antigens may be released from the device to initiate the immune response. In contrast, the current invention relies on biodegradable polymers to dispose of

the device after it has induced the desired immune response, beyond around 10 days after the immune cells within the device have been exposed to an antigen. Thus although the biodegradable polymers will have the same attributes, the two devices have utilized these properties to operate entirely differently.

Thus, despite the Examiner's assertions the current invention would not have been obvious to one off ordinary skill in the art.

The Examiner acknowledges that Barr does not teach the use of the device for generating hybridomas. However, the Examiner relies upon Andrianov to argue that would have been obvious to one of ordinary art to use the current invention to make hybridomas. As the Applicants' note above the current invention is not obvious in light of Barr and therefore the combination of Barr and Andrianov will not render the current invention obvious.

## CONCLUSIONS

Applicants respectfully request that the foregoing amendment and remarks be made of record in the file history of the instant application. Applicants estimate that the remarks and amendment made herein now place the pending claims in condition for allowance.

Respectfully submitted,

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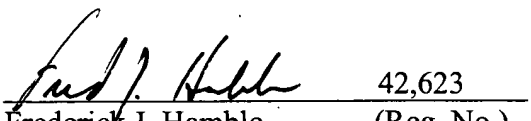
By:  42,623

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